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Hematological and Pulmonary Responses to High Altitude in Quechuas: A Multivariate Approach

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ABSTRACT This study investigates the relationships among hematological variables, pulmonary function, and age in a sample of high-altitude natives. The following anthropometric and physiological variables were examined in 77 adult Quechua males from the Peruvian Central Andes (Huancavelica, 3,680 m): height, weight, sitting height, chest diameters, chest and abdominal circumferences, forced vital capacity (FVC), forced expiratory volume at 1 sec (FEV1), peak expiratory flow (PEF), hemoglobin concentration (Hb), red blood cells (RBC), hematocrit (Htc), diastolic and systolic blood pressure, body temperature, pulmonary rate, and pulse rate. The means of these variables for the Huancavelica sample fall within the range of variability previously observed in Andean populations. Principal components analysis and canonical correlation analysis suggest that in this native Andean population: 1) aging decreases lung function but does not affect hematological features, and 2) there is a negative age-independent correlation between lung function (FVC, FEV1, PEF) and hematological traits (Hb, RBC, Htc). Am J Phys Anthropol 111:165–176, 2000. © 2000 Wiley-Liss, Inc.

The high-altitude regions of America, Asia, and Africa constitute a multistress environment inhabited by several million people. In addition to the predominant hypoxic stress, other environmental factors delineate the special nature of this habitat: cold, poor nutritional environment, high ultraviolet (UV) radiation, socioeconomic problems, and geographic isolation (Picon Reategui, 1978; Leonard, 1989a,b; Pretell, 1992; De Meer et al., 1993; Leatherman et al., 1995; Facchini et al., 1997). Nevertheless, human populations in the Andes and Himalayas have inhabited the high-altitude environment for thousands of years, while others (e.g., in North America and Central Asia) have colonized it more recently, i.e., a few centuries ago (Pawson and Jest, 1978; Bonavia, 1991; Pettener et al., 1997). This interesting framework has motivated population biologists to investigate the adaptive mechanisms to hypoxia developed by these peoples (Baker, 1976, 1978, 1996; Greksa and Beall, 1989; Moore, 1990; Monge and Leon Velarde, 1991; Greksa, 1991; Moore et al. 1998).

Studies on populations living permanently in high-altitude environments have shown some peculiarities of the respiratory, cardiovascular, and hematological systems, related to oxygen uptake, transport, and

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delivery. There is an increase in lung volumes, hemoglobin, red blood cell concentrations, and hematocrit with altitude (Hurtado, 1932, 1964; Hurtado et al., 1945; Frisancho, 1969, 1988; Mueller et al., 1978, 1979; Winslow et al., 1981; Winslow and Monge, 1987; Greksa et al., 1988; Ballew et al., 1989; Beall and Goldstein, 1990; Droma et al., 1991). This pattern of variability is generally presumed to be related to the decreased partial pressure of oxygen at high altitude.

Current studies of human adaptation to high altitude quantify genetic and developmental components of the variability shown by hematological and pulmonary characters (Greksa et al., 1985a,b; Greksa, 1996; Frisancho et al., 1995), to test their consistency with quantitative genetic models (Beall, 1993; Beall et al., 1994, 1997), and to assess possible adaptive patterns exhibited by different populations of high-altitude regions (Frisancho, 1988; Ballew et al., 1989; Greksa and Beall, 1989; Droma et al., 1991; Zamudio et al., 1993a; Beall et al., 1998). However, the relationships among the different systems involved in the uptake, transport, and delivery of oxygen have received less attention (Frisancho, 1969; Mueller et al., 1978; Winslow and Monge, 1987).

In this study, we present original anthropometric and physiological data from a native Quechua population of the Peruvian Central Andes. The purpose of this paper was to investigate, using a multivariate approach, the relationships among hematological, pulmonary, and anthropometric variables, taking into account the effects of age. We also discuss methodological aspects related to the use of multivariate statistical methods in adaptive studies.

MATERIALS AND METHODS

Sample

The sample is composed of 77 unrelated healthy adult males of the Quechua ethnic group. All are native and lifelong, high-altitude residents of the area around the city of Huancavelica, at 3,680 m or higher. The population is characterized by low rates of admixture with nonindigenous populations (Pettener et al., 1998). Seventy-three percent of the subjects are manual laborers

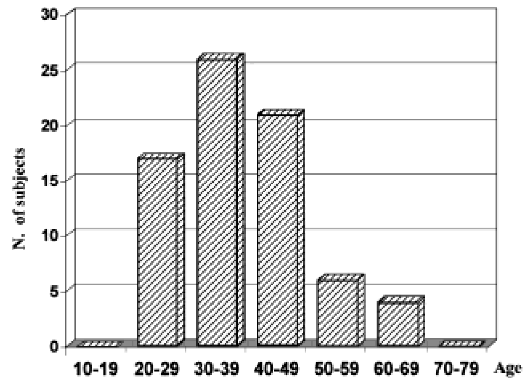

Fig. 1. Age distribution of the sample.

(mainly farmers). The mean age of the sample is 38.3 years (SD = 11.4, range 20–69 years). The age distribution is shown in Figure 1.

Anthropometric and physiological variables

All data were collected during the spring of 1994. Each subject was interviewed to verify his Quechua ethnic origin and permanent residence in the high-altitude environment and was examined to evaluate his state of health. All subjects affected by cardiovascular or respiratory diseases (including tuberculosis) in the past were excluded from the study. One individual with clinical symptoms of chronic mountain sickness was also excluded. The anthropometric and physiological variables and their respective abbreviations are presented in Table 1. All anthropometric measurements were taken by the same investigator (E.T.-S.), according to the recommendations of Weiner and Lourie (1969). The forced vital capacity (FVC), forced expiratory volume at 1 sec (FEV1), and peak expiratory flow (PEF) were measured with a portable Vitalograph-ALPHA spirometer calibrated twice a day (measurement error was always less than 2%). Each subject carried out the spirometric test twice, and the highest BTPS value was recorded. Hemoglobin concentration (Hb), red blood cells (RBC), and hematocrit (Htc) were measured separately from capillary blood samples with a portable Hemo-Flash Menarini spectrophotometer calibrated before the

TABLE 1. Anthropometric and physiometric variables investigated and respective abbreviations

Variable	Abbreviation
Age (years)	Age
Diastolic blood pressure (mm Hg)	Diastolic
Systolic blood pressure (mm Hg)	Systolic
Pulse rate (n/min)	Pulse
Respiratory rate (n/min)	Pulm
Body temperature (°C)	Temp
Forced vital capacity (liters)	FVC
Forced expiratory volume at one second (liters)	FEV1
Peak expiratpory flow (liters/min)	PEF
Weight (kg)	Weight
Height (cm)	Height
Sitting height (cm)	Sit. Height
Chest breadth (cm)	Chest B
Chest depth (cm)	Chest D
Chest height (cm)	Chest H
Abdominal circumference (cm)	CAbd
Normal chest circumference (cm)	CCNor
Maximal chest circumference (cm)	CCMax
Minimal chest circumference (cm)	CCMin
Hemoglobin concentration (g/dl)	Hb
Red blood cells (million/cc)	RBC
Hematocrit (%)	Htc

expedition. Three readings of Hb, RBC, and Htc were taken and the mean values were recorded.

Statistical analysis

The means and standard deviations were calculated for each variable. To assess changes related to aging, we calculated the Pearson correlation coefficient with age and its level of significance for each variable. The nonmetric Kolmogorov-Smirnov test was used to verify the normal distribution of the variables. We used principal components analysis (PCA) to explore the relationships between the different morphological, hematological, and pulmonary variables and age. PCA is a robust method widely used in ecology, population genetics, and biological adaptability studies (Andrews and Williams, 1973; Majumder et al., 1986; James and McCulloch, 1990; Greksa, 1992; Pettener et al., 1994; Livshits et al., 1998). It redistributes the total variance of a matrix of data among independent components (i.e., principal components, PCs). The load scores corresponding to each PC provide information about the correlations between variables involved in each PC. PCA was applied to the matrix of raw data from the 77 individuals for the 22 variables.

The variability structure resulting from PCA could be affected by adaptive and/or aging processes. To analyze the relationships between hematological and pulmonary variables independently of aging, we removed the age effect from the sample by performing a least squares linear regression for each variable on age. Residual analysis indicated the absence of any nonlinear effect. Least squares linear regression is particularly sensitive to outliers, and we used Cook's distance to identify them. This is a normalized indicator of the influence of each individual on the construction of the regression equation. All individuals with a Cook's distance higher than 0.5 for at least one variable were excluded from the multivariate analysis, leaving 72 individuals with Cook's distance values lower than 0.2. PCA was also applied to the matrix obtained with residual values from the regression equations for each variable on age, and the results were compared with those obtained from the previous PCA based on the raw data. Canonical correlation analysis (CCA), a multivariate procedure for assessing the relationship between different sets of variables, was used for further investigation of the relationship between the pulmonary and hematological variables.

RESULTS

Table 2 reports the basic statistics for all the variables, plus minimum and maximum values, correlations with age (and their respective significance levels), and regression equations using age as the independent variable. We have also included the maximum Cook's distance after removal of individuals with values higher than 0.5 and the mean of residual values. There are no variables showing significant departure from normality. The mean values of height, weight, sitting height, chest diameters, and circumferences (Table 2) indicate that body sizes in the Huancavelica sample are comparable to those reported for other Andean high-altitude populations (Tarazona-Santos et al., 1997; Frisancho et al., 1973; Beall, 1982; Leatherman et al., 1984; Greksa et al., 1984). The sitting height*100/height ratio of our sample (53.53 ± 1.3) is also comparable to that of other Andean populations (see

TABLE 2. Basic statistics, correlations, and regression on age for the examined variables[1]

	Basic statistics					Correlation with age		Regression analysis on age: Equation parameters		Regression analysis on age: Maximum Cook's distance	Regression analysis on age: Mean values of residuals
Variables	N	Mean	S.D.	Minimum	Maximum	r	*P*-level	Beta	a		
Systolic blood pressure (mm Hg)	77	104.74	10.97	80.00	130.00	0.03	0.83	0.03	103.57	0.16	0.02
Diastolic blood pressure (mm Hg)	77	69.05	8.24	50.00	90.00	0.08	0.49	0.03	67.96	0.12	−0.11
Pulse rate (n/min)	77	63.81	10.04	46.00	104.00	0.33	0.01	0.14	57.52	0.19	0.08
Respiratory rate (n/min)	75	18.92	2.41	14.00	24.00	0.03	0.80	−0.01	19.31	0.12	−0.75
Body temperature (°C)	76	36.53	0.38	35.40	37.30	−0.17	0.15	−0.01	36.73	0.19	−0.01
FVC (liters)	77	4.82	0.91	3.09	6.90	−0.40	<0.001	−0.04	6.19	0.08	0.01
FEV1 (liters)	77	3.95	0.76	2.42	5.74	−0.57	<0.001	−0.04	5.41	0.12	−0.01
PEF (liters/min)	77	499.63	137.26	186.00	824.00	0.13	0.26	−1.61	563.14	0.11	−1.01
Weight (kg)	72	60.00	6.63	41.80	74.00	0.10	0.40	0.06	57.88	0.07	−0.08
Height (cm)	77	157.91	5.56	144.50	170.90	−0.30	0.01	−1.52	163.66	0.10	−2.01
Sitting height (cm)	77	84.52	3.41	75.40	91.60	−0.30	0.01	−0.80	87.55	0.16	−0.80
Chest breadth (cm)	77	26.07	1.72	21.80	30.50	0.12	0.30	0.27	25.11	0.15	0.07
Chest depth (cm)	77	20.52	1.53	17.30	27.10	0.47	<0.001	0.49	18.63	0.07	0.10
Chest height (cm)	77	15.31	1.32	12.40	18.40	−0.17	0.16	−0.21	16.10	0.17	−0.14
Abdominal circumference (cm)	77	84.14	5.58	71.50	97.00	0.40	<0.001	1.95	76.86	0.09	−0.93
Normal chest circumference (cm)	77	92.38	4.18	85.50	101.00	0.17	0.15	0.59	90.25	0.09	−0.91
Maximal chest circumference (cm)	77	96.23	4.15	89.00	104.90	0.12	0.31	0.39	94.92	0.14	−1.14
Minimal chest circumference (cm)	77	90.38	4.18	82.00	98.60	0.25	0.03	0.94	86.85	0.09	−1.33
Hb (g/dl)	77	17.53	1.93	12.70	22.00	−0.01	0.92	−0.02	18.27	0.13	0.00
RBC (millions/cc)	77	5.27	0.55	3.70	7.00	−0.05	0.70	−0.01	5.60	0.11	0.00
Htc (%)	77	47.72	3.79	39.00	60.00	0.03	0.77	−0.03	42.90	0.10	−2.52

[1] Sample size (N), mean, standard deviation (S.D.), maximum and minimum values, correlation coefficients with age (r) and their level of significance (*P*-level), regression equation parameters on age (Beta and a), maximal Cook's distance, and mean values of residuals.

Frisancho, 1976). Therefore, for the anthropometric parameters considered, the Huancavelica sample falls within the range of variability previously observed in Andean populations.

Lung function in the Huancavelica sample was assessed through measurements of FVC, FEV1, and PEF. FVC was between 3.09–6.90 l (mean: 4.82 ± 0.91 l), and FEV1 was between 2.42–5.74 l (mean: 3.95 ± 0.76 l). There is a strong negative correlation of both FVC and FEV1 with age, whereas PEF is not significantly associated with age (Table 2). The index FVC/height (liters/meters) in the sample ranges between 1.95–4.14, with a mean value of 3.05 ± 0.52 l/m. It is also negatively correlated with age ($r = -0.38$, $P < 0.05$).

The mean values of the three hematological variables are: Hb, 17.53 ± 1.93 g/dl; RBC, 5.27 ± 0.55 millions/cc; and Htc, 47.72 ± 3.79 %. Unfortunately, we could not perform additional clinical tests to ascertain whether the lower values of Hb, RBC, and Htc in the sample were due to cases of anemia. However, the normal distributions of the Hb, RBC, and Htc values (Kolmogorov-Smirnov d values: 0.86, 0.11, and 0.08, respectively, $P > 0.20$) suggest that we are dealing with a healthy sample (Haas et al., 1988). Finally, the Huancavelica sample shows no significant correlations between hematological variables (Hb, RBC, Htc) and age (Table 2).

Multivariate analyses

Results of the PCA applied to the original data and the residual matrix are shown in Figures 2A–C and 3A–C, respectively. They report the load scores for each variable, the eigenvalues, and the percentage of total variance of the sample explained by each principal component. The first principal component from the raw matrix data, which

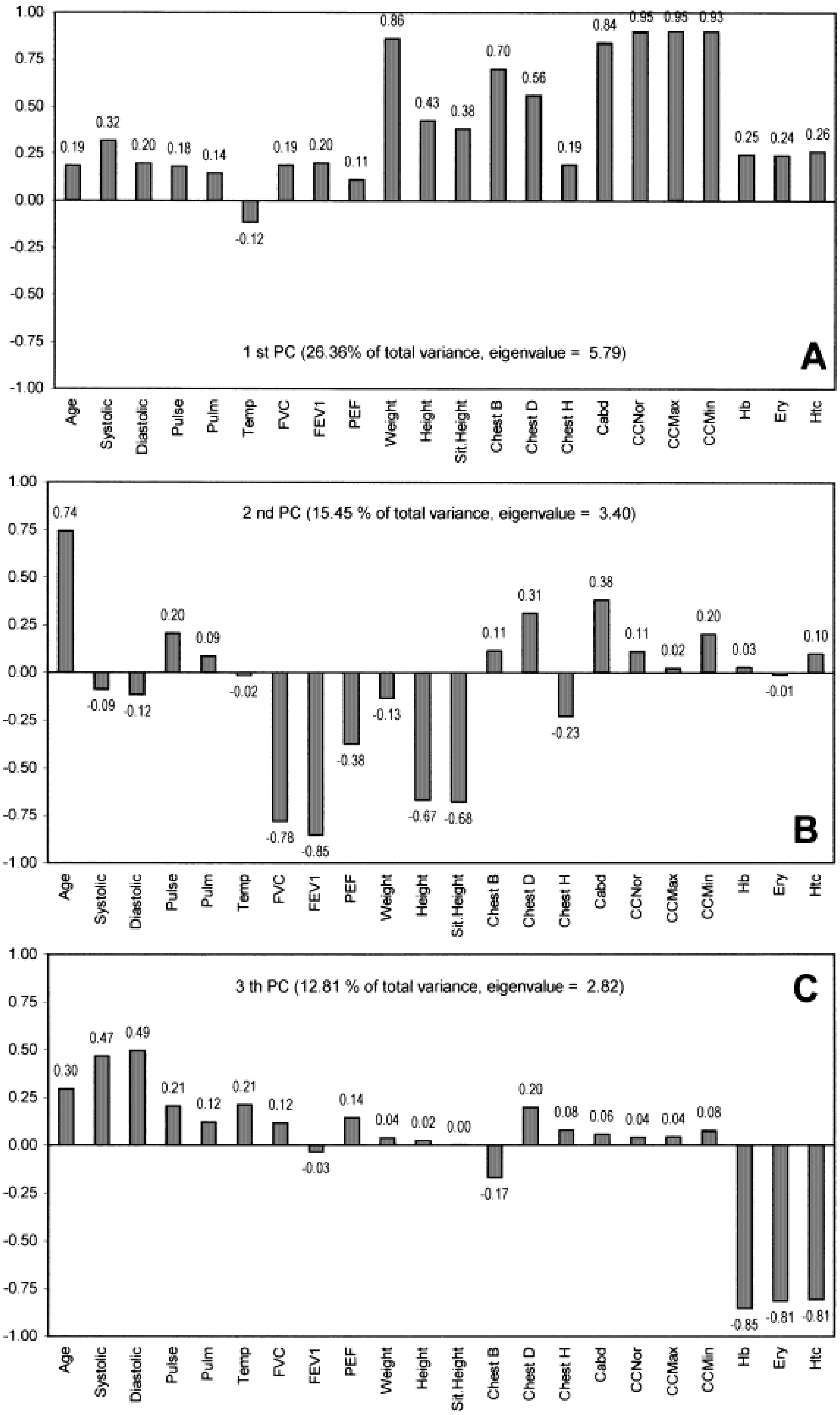

Fig. 2. Load scores of the first three principal components obtained from the original anthropometric and physiological data.

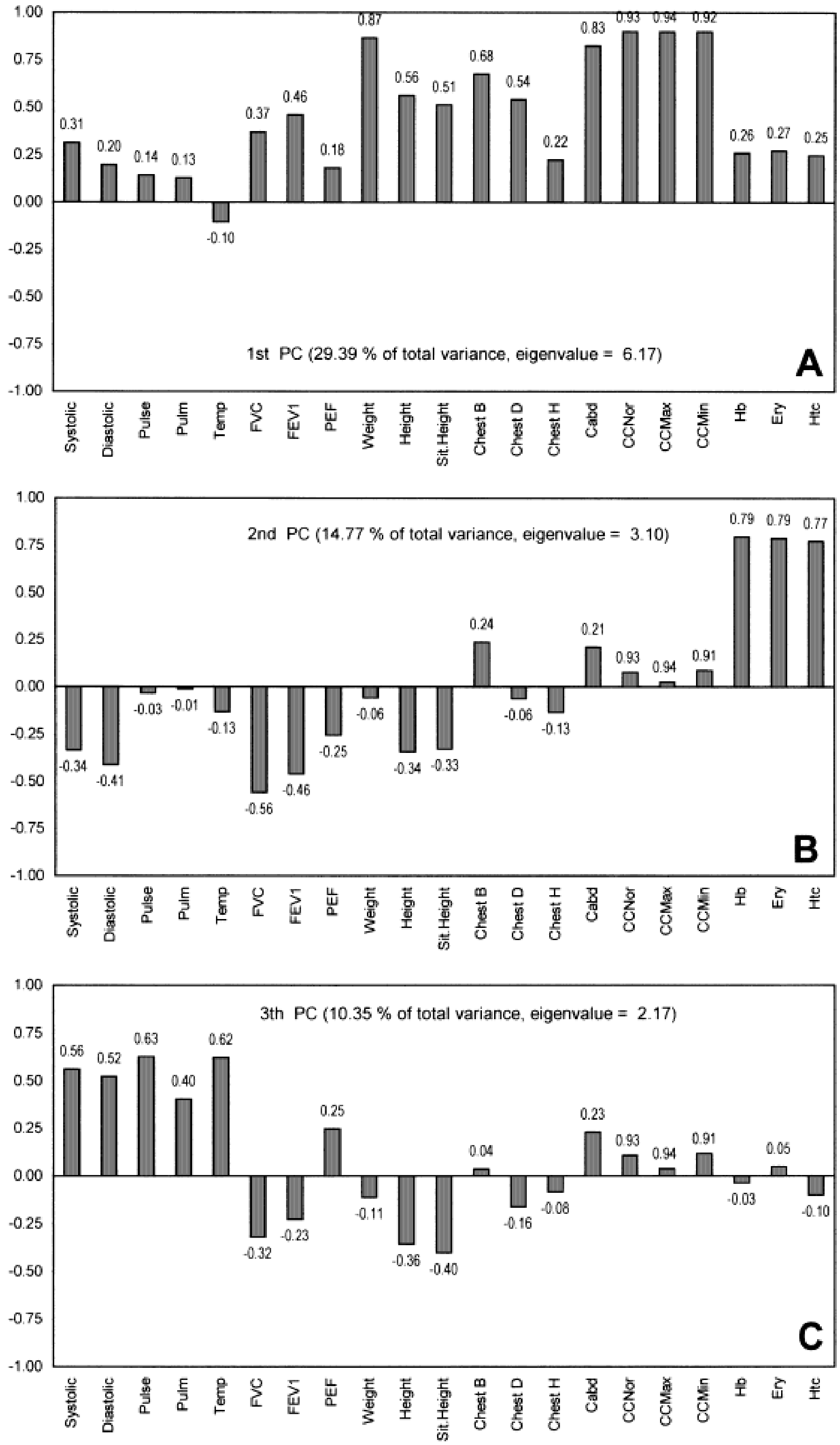

Fig. 3. Load scores of the first three principal components obtained from the matrix of the residual of the regression on age.

explains 26.36% of total variance, is a dimensional component determined by transverse anthropometric variables: chest and abdominal circumferences (load scores > 0.8), chest diameters ($0.5 <$ load scores < 0.8), and weight (Fig. 2A). The second principal component (15.45% of total variance) is determined mainly by FVC, FEV1, height, and sitting height, and is inversely correlated with age (Fig. 3B). This component clearly shows the effect of aging on lung function, in agreement with previous studies conducted in other high-altitude populations (Mueller et al., 1978; Beall et al., 1992). In our sample, chest dimensions are not highly correlated with FVC and FEV1. Although some authors have suggested a correlation between chest diameters and lung volumes during childhood (Frisancho, 1969; Mueller et al., 1978), it is probable that when growth is completed, the main determinant of lung function variability is the aging process. The load scores obtained from the second principal component indicate that the role of hematological variables within this share of variability is not relevant, suggesting their relative independence from the age-dependent decrease of lung function in our sample. In contrast, the third principal component (12.81% of the total variance) is predominantly hematological in nature, determined mainly by load scores corresponding to hemoglobin concentration, red blood cells. and hematocrit (Fig. 2C). It is difficult to interpret the variability explained by further principal components (results not shown), which explain only small portions of the total variance (lower than 9%) and could be mainly affected by background noise.

To investigate the pattern of variability when the age effect is removed, we applied PCA to the matrix of residual values obtained from the regression equations on age. The results are shown in Figure 3A–C. The first principal component (29.39% of total variance, Fig. 3A) gives the same dimensional pattern as the first component of the previous analysis. However, the second principal component (14.77% of total variance, Fig. 3B) shows interesting differences from the previous second component: there is a negative correlation between the shares of variability of hematological variables and lung volumes (load scores: FVC, −0.56; FEV1, −0.46; Hb, 0.79; RBC, 0.79; Htc, 0.77). Therefore, when the effect of age is removed, the pattern of variability of our sample changes. The third principal component is similar to the previous fourth principal component (not shown). It accounts for 10.3% of total variance and could be related to systemic circulation (Fig. 3C).

TABLE 3. Canonical correlations between hematological (Hb, RBC, Htc) and pulmonary (FVC, FEV1, PEF) variables

	Canonical correlations		
	First	Second	Third
Raw data	0.400 (P = 0.04)	0.184	0.152
Linearly adjusted data	0.420 (P = 0.01)	0.206	0.133
Nonlinearly adjusted data	0.436 (P = 0.01)	0.230	0.185

We used canonical correlation analysis (CCA) to further investigate and confirm this specific negative correlation between the pulmonary (FVC, FEV1, PEF) and hematological (Hb, RBC, Htc) variables, emerging when age effect is removed. Table 3 reports the results of the CCA of raw data, residual data, and data nonlinearly (loess) adjusted by age. Canonical correlation coefficients can assume values between 0 and 1, and the sign of correlation should be determined by other methods. In this case, the second PC attests that correlation is negative. All first canonical correlations between the pulmonary and hematological variables are between 0.40 and 0.44. The significance of the first canonical correlation (P = 0.04 for raw data and P = 0.01 for adjusted data) was estimated by simulation from two sets of three normally distributed variables (i.e., Hb, RBC, Htc, and FVC, FEV1, PEF) having the same correlations as the pulmonary and hematological variables in the sample. Therefore, CCA on raw and linearly and nonlinearly adjusted-by-age data strongly confirms the age-independent and negative correlation between pulmonary and hematological variables.

DISCUSSION

The mean values of the anthropometric variables indicate that the body size of the Huancavelica sample falls within the range

TABLE 4. Hematological variables in different high-altitude Andean samples

Place	Altitude (m)	Ethnic group	Age composition of the sample	Sample size	Hb (g/dl)		RBC		Htc (%)		Reference
					Mean	S.D.	Mean	S.D.	Mean	S.D.	
Rural samples											
Huancavelica	3,680	Quechua	38.2 ± 11.3	77	17.5	1.0	5.3	0.0	47.7	3.8	This research
Murillo, Bolivia	3,900	Aymara	38 ± 2.0	91	19.1	0.1					Beall et al., 1998
Ollague, Chile	3,700	Quechua	27.3 ± 5.9	24	18.0	1.0	6.1	1.0	52.2	4.0	Winslow et al., 1981
Visviri, Chile	4,100	Aymara	6–90[1]	233	17.2	1.0			49.9	5.0	Clench et al., 1982
Nuñoa	4,200	Quechua	34.7	44	17.3	1.0	5.6	0.0	51.4	3.0	Garruto and Dutt, 1983
Guallatiri, Chile	4,260	Aymara	6–90[1]	60	17.6	1.0			51.8	6.0	Clench et al., 1982
Parinacota, Chile	4,460	Aymara	6–90[1]	70	18.4	1.0			54.3	6.0	Clench et al., 1982
Caquena, Chile	4,600	Aymara	6–90[1]	98	18.7	1.0			54.3	6.0	Clench et al., 1982
Urban samples											
Santa Cruz	400	Aymara	23.0 ± 7.0	84	14.5	1.0	4.4	0.0	41.2	4.0	Arnaud et al., 1979
Jujuy Argentina	1,260	Mixed	36.7	32	16.0	0.0	5.0	0.0	47.9	0.0	Chiodi and Pozzi, 1961
Volcan	2,078	Mixed	34.4	32	16.9	0.0	5.4	0.0	50.8	0.0	Chiodi and Pozzi, 1961
Huamahuaca	2,939	Mixed	29.8	45	16.8	0.0	5.5	0.0	51.1	0.0	Chiodi and Pozzi, 1961
La Paz	3,600	Aymara	Older	11	16.7						Beall et al., 1992
La Paz	3,600	Aymara	Young	14	17.5						Beall et al., 1992
La Paz	3,600	Aymara	22.0 ± 3.0	85	18.2	1.0	5.7	0.0	51.8	2.0	Arnaud et al., 1979
La Paz	3,600	Mixed	35.0	600	19.0				54.0		Cited by Beall et al., 1992
La Paz	3,700	Mixed		499	18.8	1.0					Tufts et al., 1985
Puno	3,840	Quechua		40	17.2	1.0	5.7	0.0	51.2		Frisancho et al., 1973
Mining communities											
Ancos	1,200	No data		104	14.8	1.0					Cosio, 1972
Arequipa	2,300	No data		168	15.4	1.0					Cosio, 1972
Chuquicamata	2,800	Mixed		270	17.4	1.0					Santolaya et al., 1981
Pasto Bueno	3,475	Mixed		408	18.0	1.0					Cosio, 1972
Buldibuyo	3,720	No data		271	17.8	1.0					Cosio, 1972
La Oroya	3,740	Quechua		40	18.8	1.0					Hurtado et al., 1945
Mina Aguiar	3,990	Mixed	37.8	15	18.0	0.0	5.8	0.0	53.9	0.0	Chiodi and Pozzi, 1961
Mina Aguiar	4,515	Quechua	22–57[1]	96	19.3	1.0					Chiodi, 1978
Mina Aguiar	4,515	Mixed	33.8	84	19.4	0.0	6.5	0.0	59.5	0.0	Chiodi and Pozzi, 1961
Morococha	4,540	Quechua		83	20.1	2.0					Hurtado et al., 1945
Morococha	4,540	Mixed	36.0 ± 11.00	46	20.2	2.0			61.0	8.0	Winslow et al., 1981

[1]Age range.

of variability previously observed in Andean populations.

Concerning the variability of FVC in Andean populations, a comparison between our sample and Northern Chileans studied by Mueller et al. (1978) has been performed elsewhere (Tarazona-Santos et al., 1997). If we consider only the 20–29-year-old age class ($N = 17$, $FVC = 5.12 \pm 0.83$ l) for comparison with other similar age-distributed samples of Andean populations, the Huancavelicans do not differ significantly from young Aymaras of La Paz (3,600 m, Beall et al., 1992) or from Quechuas of Nuñoa (4,400 m, Frisancho, 1969).

Hemoglobin concentration has been extensively investigated in several high-altitude populations. Table 4 summarizes the values of hematological variables from different studies in the Andes. Hemoglobin concentration of the Huancavelica sample does not differ significantly from other native Quechua samples living at comparable altitudes (Table 4), such as the rural sample of Ollague, Chile (Winslow et al., 1981) and the urban sample of Puno (Frisancho et al., 1973). Our sample has significantly lower Hb values than Quechuas of the mining populations of La Oroya (3,740 m, Hurtado et al., 1945) and Pasto Bueno (3,475 m, Cosio, 1972).

Principal components analysis (PCA) was used to explore the variability structure of our typical Quechua high-altitude sample with respect to physiological, aging, and anthropometric variables. In particular, we were interested in investigating relationships between lung function and hematological features, since they are presumed to be important in adaptation to a hypoxic environment. PCA applied to the raw matrix of data suggests that aging exerts a strong influence on the relationships between these variables, as indicated by the high load score shown by age in the second principal component. Therefore, apart from the dimensional

component (first principal component), the age distribution of the sample is the main determinant of the variability structure. The analysis, which accounts for the adaptive components to high altitude, suggests a decrease of lung function during aging, independent of the variability observed in hematological responses. At this altitude (3,680 m), we found no correlation between hematological variables and age in our sample (N = 77), as also indicated by a bivariate analysis (Table 2). This agrees with previous findings in the highlands: Chiodi (1978) at 4,515 m, Arnaud (1982) at 3,600 m, Garruto and Dutt (1983) at 4,200 m, Beall and Goldstein (1990) at 5,050 m, and Beall et al. (1992) at 3,600 m.

Principal components analysis applied to the age-adjusted (i.e., regression residuals) matrix shows that removal of the age effect partially modifies the pattern of variability observed previously. This modification is relevant because it concerns pulmonary and hematological variables, which are functional indicators of systems involved in oxygen uptake and delivery, important processes in the adaptation to a hypoxic environment. The results of the PCA indicate that aging causes decreased lung function but does not affect hematological features and suggest an age-independent negative correlation between lung functions (FVC, FEV1, PEF) and hematological traits (Hb, RBC, Htc). The results also show that variability related to body dimensions (i.e., first principal component of the raw data analysis) and the age distribution of the sample (i.e., second principal component of the raw data analysis) could hide the age-independent relationships between pulmonary and hematological variables. Hence, it is useful to remove those factors. However, removal of the age effect should be treated with caution in order to identify the proportions of the total variance unexplained and explained by the age components. Specifically, the sample size and the age distribution of the sample could affect the results obtained by the least squares regression, and the PCA may amplify these errors. For these reasons, we examined carefully the scatterplot of each variable on age and performed a residual analysis in order to avoid biases caused by nonlinear effects. As expected, when the age effect has been correctly removed by a linear regression, all the residual distributions, with only the exception of systolic and diastolic blood pressure, fit the normal distribution (Kolmogorov-Smirnov test, $P > 0.05$). Moreover, mean values of residuals for all the variables are very near to zero (Table 2). In view of the sensitivity of least squares regression to outliers, we also controlled for Cook's distances so as to avoid this other source of bias. This cautionary procedure should exclude from the multivariate analysis any individuals eventually affected by anemia. If removal of the age effect has been adequately performed, PCA allows an unbiased detection of the relationships among pulmonary and hematological variables. Furthermore, canonical correlation analysis (CCA) confirms the negative relationship between these variables, and the simulation approach shows the statistical significance of this finding, even if the sample size is not very large.

On the basis of this significant negative correlation between lung function and hematological variables suggested by PCA and CCA, we can hypothesize the existence of different individual adaptive responses based, alternatively, on lung function or hematological features. These results suggest that high-altitude peoples could have a certain amount of within-population variability in adaptive patterns (i.e., different combinations of characters), in addition to the variability in the single characters. Several studies suggest that environmental and genetic factors account for the variability in lung function, hematological, and other variables in Andean (Chakraborty et al., 1983; Frisancho et al., 1995; Greksa, 1996; Beall et al., 1998) and Tibetan (Niermeyer et al., 1995; Beall et al., 1997, 1998; Moore et al., 1998) populations. Therefore, if some genotypes confer higher fitness than phenotypes determined by developmental adaptation, natural selection could reasonably have operated, given that the Andean and Tibetan ancestors colonized the highlands at least 10,000 years ago. Furthermore, there is evidence of genetic adaptation in these populations (Beall, 1993; Beall et al., 1997; Winslow et al., 1981; Moore et al., 1992, 1998;

Zamudio et al., 1993b; Curran et al., 1998). We would ask if the observed patterns (i.e., different associations of pulmonary and hematological characters leading to a negative correlation at population level) are adaptive and could also reasonably be under genetic control and thus eventually be formed by natural selection. We have no evidence for this but it is theoretically possible, even though models of selection of multivariate characters indicate that the highest fitness is reached slowly when characters are correlated (e.g., lung function and hematological variables in this study) (Hartl and Clark, 1997).

In this investigation, we used a combination of multivariate statistical methods. The use of PCA allowed us to explore relationships among a wide set of anthropometric and physiologic variables. The results of the PCA prompted further investigation (by canonical correlation analysis), focusing on the relationships between pulmonary and hematological variables. In our native Quechua sample living at 3,680 m, we found a decrease of FVC and FEV1 with age, but not associated with an increase in hemoglobin concentration, red blood cells, or hematocrit levels. Our results, based on a multivariate approach and adequate control of age and morphological variables, strongly suggest an inverse correlation between hematological and pulmonary responses, independent of age. A negative correlation between FVC and hemoglobin concentration has been shown previously in a Phala population by Beall and Goldstein (1990) and in a Kazak population (2,100 m) by Pettener et al. (1994), although these studies did not control for the effect of age. Further studies are needed to ascertain whether the variability structure and in particular the negative correlation between pulmonary and hematological variables detected in our Andean Quechua sample are ethnic- or altitude-specific, and the possible adaptive nature of this pattern.

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